UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,812	09/26/2006	Robert Kallmeier	2006_1236A	4681

513 7590 03/23/2009

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
NAVARRO, ALBERT MARK	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
03/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,812	KALLMEIER ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants preliminary amendment filed September 6, 2006 has been received and entered. Claims 1-57 have been cancelled, and new claims 58-75 have been added. Accordingly, claims 58-75 are pending in the instant application.

Claim Objections

1. Claim 58 is objected to because of the following informalities:

Claim 58 recites "comprising at least ***a a*** VH, CH2 and...". An obvious typographical error. Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. Claim 63 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 63 recites a furin endoprotease or lymphoma proprotein convertase or "a functional variant thereof."

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails

to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "functional variant" alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. There is no teaching regarding which amino acids can vary from a furin endoprotease/lymphoma proprotein convertase, and still result in a protein that retains activity. Thus, applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."

Applicant is reminded that Vas-Cath make clear that the written description provision of 35 USC 112 is severable from its enablement provision.

Furthermore, in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus by only their functional activity does not provide an adequate written description of the

genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

Applicants are directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, the guidelines can be found at the following link on the USPTO Internet in "Patents Guidance"

http://www.uspto.gov/web/patents/guides.htm

3. Claim 63 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 63 is vague and indefinite in the recitation of "a functional variant." For instance, what function is being measured? Furthermore, what level of function must be retained to be considered functional (e.g., 90%, 70%, 50%, etc)? Without a clear definition for the term "functional variant" one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 58-65, 68-71, and 75 are rejected under 35 U.S.C. 102(e) as being anticipated by Fang et al.

The claims are directed to a method for producing an immunoglobulin having Fc receptor activity and/or complement activity which immunoglobulin molecule when secreted from a vertebrate host cell comprises at least a first and a second polypeptide chain wherein the first polypeptide is an Ig-light chain (L) comprising at least a VL and a CL domain and in that the second polypeptide is an Ig-Heavy chain (H) comprising at least a VH, CH2 and CH3 domain and a hinge domain, comprising the steps of expressing in a vertebrate host cell having Golgi only or late Golgi only resident furin family endoprotease activity a fusion polypeptide comprising a secretion targeting sequence directing the polypeptide to the secretory pathway and further comprising at least the said first and second polypeptide sequences and at least one cleavage site for the said endoprotease activity and wherein the fusion polypeptide comprises the sequences of said first and second polypeptide separated by a linker and having the

fusion polypeptide cleaved in the cells by the furin family endoprotease activity into the first and second polypeptide chains and harvesting the secreted immunoglobulin.

Fang et al (US Patent Number 7,485,291) disclose of single vector constructs for expression of a functional antibody molecule. (See abstract). Fang et al further set forth that the expression is a full length antibody. (See detailed paragraph 13). Fang et al further set forth of proteolytic cleavage sites inserted between the heavy chain and light chain to include furin cleavage sites. (See detailed paragraph 67; SEQ ID NO: 12). Fang et al further disclose of expressing and harvesting the secreted immunoglobulins from vertebrate host cells. (See Examples).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 58-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fang et al in view of Heinrikson et al, Sgarlato and Huston et al.

The claims are directed to a method for producing an immunoglobulin having Fc receptor activity and/or complement activity which immunoglobulin molecule when secreted from a vertebrate host cell comprises at least a first and a second polypeptide chain wherein the first polypeptide is an Ig-light chain (L) comprising at least a VL and a CL domain and in that the second polypeptide is an Ig-Heavy chain (H) comprising at least a VH, CH2 and CH3 domain and a hinge domain, comprising the steps of expressing in a vertebrate host cell having Golgi only or late Golgi only resident furin family endoprotease activity a fusion polypeptide comprising a secretion targeting sequence directing the polypeptide to the secretory pathway and further comprising at least the said first and second polypeptide sequences and at least one cleavage site for the said endoprotease activity and wherein the fusion polypeptide comprises the sequences of said first and second polypeptide separated by a linker and having the fusion polypeptide cleaved in the cells by the furin family endoprotease activity into the first and second polypeptide chains and harvesting the secreted immunoglobulin, wherein the host cell is CHO, a linker of arginine and lysine is used, or a linker of glycine is used.

The teachings of Fang et al are set forth above.

Fang et al do not teach of CHO host cells, a linker comprising arginine and lysine, or a linker comprising glycine.

Heinrikson et al (US Publication2004/0171535) set forth that it was routine in the art to express antibody constructs in suitable mammalian host cells such as CHO. (See paragraph 213).

Sgarlato (US Patent 5,935,824) set forth that preferred linkers are susceptible to protease cleavage and include lysine and arginine residues. (See summary and SEQ ID NO: 78-80).

Huston et al (US Patent Number 5,258,498) set forth that linkers preferably comprise amino acids having unreactive side groups (e.g., glycine). (See Summary).

Given that Fang has disclosed of producing immunoglobulin light chains and heavy chains separated by a linker containing a cleavage site for furin endoprotease in a vertebrate host cell, it would have been prima facie obvious to substitute CHO as the host cell, or linkers containing lysine/arginine or glycine as taught by Heinrikson et al, Sgarlato and Huston et al. Each of the above substitutions represents nothing more than an alternative embodiment yielding the same predictable result.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Navarro/
Primary Examiner, Art Unit 1645
March 18, 2009